REMARKS

Summary of the Invention

The invention, as described by the present claims, features a method for detecting an increased risk of developing Down's Syndrome in an embryo or fetus by detecting the presence of a homozygous A66G methionine synthase reductase (MTRR) polymorphism in the embryo or fetus, or in a future female parent of the embryo or fetus. The invention also features a method for detecting an increased risk of cardiovascular disease in a mammal by detecting the presence of a homozygous A66G MTRR polymorphism in the mammal. Also featured is a method for detecting an increased risk of developing a neural tube defect in a mammalian embryo or fetus by detecting, in a future female parent of the embryo or fetus, a homozygous A66G MTRR polymorphism and a low serum cobalamin level, or by detecting, in the embryo or fetus, or in a future female parent of the embryo or fetus, a homozygous A66G MTRR polymorphism and a homozygous C677T methylenetetrahydrofolate reductase (MTHFR) polymorphism.

Summary of the Office Action

Claims 6-9, 11-21, 35-39, and 42-54 are pending. Claims 12, 15-20, and 45-49 are withdrawn from consideration. Claims 6-9, 11, 13, 14, 21, 36, and 38 are rejected under 35 U.S.C. § 112, second paragraph, for lack of clarity. Claims 6-9, 11, 13, 14, 21, 35-39, 42-44, and 50-54 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. By this reply Applicants cancel claims 21, 38, 39, and 44, amend claims 6, 7, 11, 13, 14, 35, 36, 42, 50-52, and 54, add new claims 55-59, and address each of the Examiner's rejections below.

Support for the Amendment

Support for the amendment to claims 6, 7, 11, 13, 14, and 36 is found in prior claims 6, 7, 11, 13, 14, and 36 and in the specification on, e.g., page 63, line 4, through page 64, line 1. Support for the amendment to claims 35 and 42 is found in prior claims 35 and 42 and in the specification on, e.g., page 64, line 4, through page 68, line 23. Support for the amendment to claims 50-52 and 54 is found in prior claims 50-52 and 54 and in the specification on, e.g., page 58, lines 15-18. Support for new claims 55-59 is found in the specification on, e.g., page 58, line 5, through page 59, line 22. No new matter has been added by the amendment.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 6, 7-9, 11, 13, 14, 21, 36, and 38 are rejected under 35 U.S.C. § 112, second paragraph, for lack of clarity. The Examiner states that there is insufficient antecedent basis for the limitations "said neural tube defect" in line 8 of claim 6 and "developing a neural tube defect" in line 6 of claim 11. Applicants have amended claims 6 and 11 to remove these phrases. Therefore, the rejection of claims 6 and 11, and claims dependent therefrom, should be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 6-9, 11, 13, 14, 21, 35-39, 42-44, and 50-54 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner states that the specification:

> does not reasonably provide enablement for a method for detecting an increased risk of developing a NTD, Down's Syndrome, hyperhomocysteinemia, cancer or cardiovascular disease in any mammalian fetus or embryo by detecting any heterozygous or homozygous MTRR polymorphism in either or both future parents of said embryo or fetus, or in said embryo or fetus. Office Action, pp. 2-3.

In the interest of expediting prosecution of the claims, Applicants have cancelled claims 21, 38, 39, and 44, amended claims 6, 7, 11, 13, 14, 35, 36, 42, 50-52, and 54, and added new claims 55-59, so that the presently pending claims, which are directed to a method for detecting an increased risk of developing Down's syndrome (claims 6-9, 11, 13, 14, and 36), a method for detecting an increased risk of cardiovascular disease (claims 35, 37, 42, and 43), and a method for detecting an increased risk of developing a neural tube defect (claims 50-59), recite subject matter deemed enabled by the Examiner (discussed below). For the reasons discussed below, these amendments overcome the present rejection of claims 6-9, 11, 13, 14, 21, 35-39, 42-44, and 50-54 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

Method for Detecting an Increased Risk of Developing Down's Syndrome is Enabled

Claims 6-9, 11, 13, 14, and 36, as presently amended, are directed to a method for detecting an increased risk for a mammalian embryo or fetus to develop Down's syndrome. The method entails detecting the presence of a homozygous A66G MTRR polymorphism in the embryo or fetus or in a female parent of the embryo or fetus. Present claims 6-9, 11, 13, 14, and 36 satisfy the enablement requirement of 35 U.S.C. § 112 because the specification clearly teaches how to make and use the invention recited in these claims. As evidence, Applicants direct the Examiner to page 61, lines 3-23, of the specification, which teaches that mothers of

Down's syndrome babies have a significant 2.49-fold greater likelihood of having a homozygous A66G MTRR polymorphism, and thus, detection of the homozygous A66G MTRR polymorphism in a mother indicates an increased risk that her embryo or fetus will develop Down's syndrome. As is acknowledged by the Examiner (Office Action, pp. 4-5), this teaching of the specification reasonably provides enablement for the detection of an increased risk of developing Down's syndrome in an embryo or fetus by detecting the homozygous A66G MTRR polymorphism in the mother of the embryo or fetus, as is recited in claims 6-9, 11, 13, 14, and 36, as presently amended.

The specification also teaches that a mammalian embryo or fetus can be tested directly for an increased risk for developing Down's syndrome. The specification states that the homozygous A66G MTRR polymorphism is useful as a genetic marker for determining an increased risk of developing Down's syndrome and that the presence of this marker indicates such an increased risk, whether the marker is detected in the mother of an embryo or fetus, or in the embryo or fetus directly (page 61, lines 3-23, of the specification; see specifically lines 20-22). Therefore, this aspect of the invention, recited in claims 6-9, 11, 13, 14, and 36, is also clearly enabled by the specification. Because the specification clearly teaches how to make and use the invention recited in claims 6-9, 11, 13, 14, and 36, as presently amended, Applicants respectfully request that the rejection of claims 6-9, 11, 13, 14, and 36 under 35 U.S.C. § 112, first paragraph, for lack of enablement be withdrawn.

Method for Detecting an Increased Risk of Cardiovascular Disease is Enabled

The specification also clearly teaches how to make and use the method of present claims 35, 37, 42, and 43, which are directed to a method for detecting an increased risk of cardiovascular disease by detecting the presence of a homozygous A66G MTRR polymorphism in a mammal. Applicants direct the Examiner to page 62, line 2, through page 66, line 16, of the specification, which teaches that males and females have a significantly higher risk of developing coronary artery disease when they have a homozygous A66G MTRR polymorphism and a determination of that risk can be made by detecting the presence of the homozygous A66G MTRR polymorphism. The specification clearly indicates that the A66G MTRR polymorphism can be used as a genetic marker to screen individuals for an increased risk of developing cardiovascular disease (see, e.g., page 64, lines 12-21). Therefore, the specification fully enables a method for detecting a mammal's increased risk of cardiovascular disease by detecting the presence of a homozygous A66G MTRR polymorphism in that mammal, as is recited in claims 35, 37, 42, and 43; a fact which is acknowledged by the Examiner (Office Action, p. 3). Because the specification clearly teaches how to make and use the invention recited in claims 35, 37, 42, and 43, as presently amended, Applicants respectfully request that the rejection of claims 35, 37, 42, and 43 under 35 U.S.C. § 112, first paragraph, for lack of enablement be withdrawn.

Method for Detecting an Increased Risk of Developing a Neural Tube Defect is Enabled

Finally, the specification teaches how to make and use the method of present claims 50-59, which are directed to a method for detecting an increased risk of developing a neural tube

defect in an embryo or fetus by detecting the presence of a homozygous A66G MTRR polymorphism and low serum cobalamin level in a female parent of the embryo or fetus (claims 50-54), or by detecting the presence of a homozygous A66G MTRR polymorphism and a homozygous C677T methylenetetrahydrofolate reductase (MTHFR) polymorphism in a female parent of the embryo or fetus (claims 55-59). With respect to claims 50-54, the specification teaches that there is a significant 5-fold increase in risk for the development of a neural tube defect in an embryo or fetus when the mother of that embryo or fetus has a homozygous A66G MTRR polymorphism and a low cobalamin level, and further, that a determination of that increased risk can be made by detecting the homozygous A66G MTRR polymorphism and low cobalamin level in the mother (see page 12, line 8, through page 13, line 20, and page 55, line 24, through page 56, line 17, of the specification). With respect to claims 55-59, the specification teaches that detection of homozygous A66G MTRR and C377T MTHFR polymorphisms in either the embryo or fetus or the mother indicates an increased risk for the embryo or fetus of developing a neural tube defect (see page 12, line 8, through page 13, line 20, and page 56, line 21, through page 57, line 14, of the specification). Therefore, the specification fully enables a method for detecting an increased risk of developing a neural tube defect in an embryo or fetus by detecting either a homozygous A66G MTRR polymorphism and a low cobalamin level or homozygous A66G MTRR and C377T MTHFR polymorphisms in the embryo or fetus or the mother of the embryo or fetus. Again, the enablement of claims 50-54, as presently amended, and new claims 55-59 is acknowledged by the Examiner in the Office Action (Office Action, p. 3). Because the specification clearly teaches how to make and use the invention recited in claims

50-59, Applicants respectfully request that the rejection of claims 50-54 under 35 U.S.C. § 112, first paragraph, for lack of enablement be withdrawn, and that this rejection not be applied to new claims 55-59.

CONCLUSION

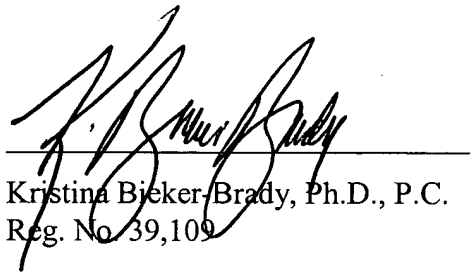
On the basis of the foregoing amendment and remarks, Applicants respectfully submit that present claims 6-9, 11, 13, 14, 35-37, 42, 43, and 50-59 are in condition for allowance, and a notification to that effect is respectfully respected.

Enclosed is a petition to extend the period for replying for one month, to and including November 2, 2004.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: November 2, 2004



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